

PMS82

FACTORS ASSOCIATED WITH INITIATION OF HIGH-DOSE DULOXETINE AMONG PATIENTS WITH OSTEOARTHRITIS

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OBJECTIVES: To identify pre-treatment predictors associated with high initiating doses of duloxetine therapy for patients with osteoarthritis (OA). **METHODS:** Patients with OA diagnosis who initiated duloxetine between November 1, 2010 to March 31, 2011 were selected from a medical and pharmacy claims database. The dispense date of the first duloxetine prescription preceded by at least a 90-day gap in medication supply was defined as the index date. Comorbidities and prior medication use were assessed during six months prior to the index date. Multiple logistic regression models were performed to identify predictors of initiating duloxetine: 1) <60mg versus 60mg, and 2) >60mg versus 60mg. **RESULTS:** A total of 2034 OA patients (mean age 63.7 years; 75.5% female) who initiated duloxetine were identified. Common comorbidities included hypertension (57.4%), depression (35.3%) and diabetes (29.4%). Common pain medications used prior to duloxetine initiation were opioids (71.5%, 69.4% and 16.5% on short- and long-acting opioids, respectively), antidepressants (52.4%), and non-steroidal anti-inflammatory drug (NSAIDs, 36.5%). Of the duloxetine initiators, 50.3% started on 60mg, 38.7% <60mg and 10.9% >60mg. Compared to patients 18-44 years old, patients 75+ years old were more likely to start on a dose <60mg (Odds Ratio [OR]: 1.89, 95% Confidence Interval [CI]: 1.19-3.01). Patients with prior use of opioid (OR: 0.75, 95% CI: 0.60-0.94) or hypertension (OR: 0.74, 95% CI: 0.60-0.92) were less likely to start on <60mg, whereas patients with prior use of NSAIDs (OR: 1.24, 95% CI: 1.01-1.53) or malignancy (OR: 1.53, 95% CI: 1.06-2.21) were more likely to start on <60mg. Patients with prior use of duloxetine (OR: 1.67, 95% CI: 1.08-2.57) or depression (OR: 1.61, 95% CI: 1.12-2.31) were more likely to start on a dose >60mg. **CONCLUSIONS:** Most of the patients initiated duloxetine at 60mg/day. Presence of selected comorbidities and prior use of medications were associated with higher starting dose of duloxetine among OA patients.

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ADHERENCE AND URIC ACID GOAL ATTAINMENT WITH URATE LOWERING THERAPY IN PATIENTS WITH GOUT

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OBJECTIVES: Evaluate patient and prescriber characteristics associated with gout patients newly initiating allopurinol; evaluate adherence within this population. **METHODS:** Retrospective study of gout patients was conducted using Kaiser Permanente Southern California health care data. Patients aged 18 years and older with a diagnosis of gout (ICD9 274.xx) and allopurinol prescription from January 1, 2007 to June 31, 2010 were included. Incident allopurinol users were defined as patients that had no allopurinol prescription within 12 months prior to the 1st gout diagnosis (index date). Patients had at least 12 months of follow up after their 1st allopurinol prescription. Descriptive statistics such as age, gender, race, co-morbid conditions, concomitant medications, prescriber specialty, and allopurinol dose adjustment were calculated comparing patients at sUA goal (<6mg/dl) or not at sUA goal. MPR mean and adherence was measured using the medication possession ratio (MPR) over the follow up time period and was defined as > 80%. **RESULTS:** A total of 9288 gout patients were identified as incident allopurinol users (mean age 60 years, men 78%). All patients had at least one comorbid condition with the following conditions being the most common: hypertension (73%), chronic kidney disease (32%), and diabetes (25%). Hydrochlorothiazide (21%) and furosemide (17%) were the most commonly utilized concomitant medications. At the end of observation, 2,749 patients (30%) were at sUA goal (mean age 63 years, men 71%) versus 6539 patients not at goal (mean age 59 years, men 81%). The mean MPR for patients at goal was 92% versus 77% for patients not at goal. A total of 1793 patients (65%) were adherent and at goal versus 40% were adherent but not at goal. **CONCLUSIONS:** Sixty percent of incident allopurinol users do not have UA goal attainment and are less adherent. Efforts need to be made to improve adherence to better obtain goal attainment.

MUSCULAR-SKELETAL DISORDERS – Research on Methods

PMS84

DERIVATION OF SEVERITY INDEX FOR RHEUMATOID ARTHRITIS AND ITS EFFECT ON HEALTH CARE OUTCOMES

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OBJECTIVES: To develop a claims-based severity index for rheumatoid arthritis (RA) using large US claims data. **METHODS:** Adult patients with at least two RA diagnoses 2 months apart were identified from a large US claims database (10/1/2008-09/30/2009). Patients were required to have at least 12 months continuous health plan enrollment before and after the index date (first RA diagnosis date). A severity index for rheumatoid arthritis (SIFRA) was developed by calculating a weighted sum of 47 RA-related indicators including laboratory, clinical and functional status, extra-articular manifestations, surgical history, and medications assessed by an expert Delphi panel of six rheumatologists. Two versions of SIFRA were derived for patients with and without laboratory information. Correlations between SIFRA and previously validated claims-based indexes for RA severity (CIRAS), and other traditional comorbidity indexes were calculated. The relationship

between SIFRA and health care costs was also examined using histograms. **RESULTS:** The Spearman's rank correlations between SIFRA and CIRAS were 0.525 for SIFRA without laboratory data and 0.539 for SIFRA with laboratory data. The correlations between SIFRA and the Charlson Comorbidity Index (0.1503 without, 0.1135 with laboratory data), Elixhauser Index (0.105 without, 0.079 with laboratory data) and Chronic Disease Score (CDS) (0.255 without, 0.239 with laboratory data) were low. Histograms showed that patients in the upper tercile of SIFRA incurred \$9,123 more all-cause health care costs and \$1,326 more RA-related health care costs than patients in the lower tercile of SIFRA. **CONCLUSIONS:** SIFRA was found to have moderate correlations with the previously validated CIRAS score, and demonstrated evidence of being a significant determinant of total and RA-related health care costs for RA patients. This study suggests that SIFRA could be an important methodological tool to control for severity in RA-related outcomes research.

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WHY THE FINDINGS OF PUBLISHED RHEUMATOID ARTHRITIS MULTIPLE TREATMENT COMPARISONS ARE SO DIFFERENT - AN OVERVIEW OF RECURRENT METHODOLOGICAL SHORTCOMINGS

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OBJECTIVES: To methodologically review the published literature on rheumatoid arthritis multiple treatment comparison meta-analysis (MTCs). To identify methodological issues that can explain the substantial discrepancies in the findings of these MTCs. **METHODS:** We searched MEDLINE for rheumatoid arthritis multiple treatment comparisons. Following the PRISMA guidelines, we extracted a large set of methodological items from the identified reviews. These included, but were not limited to, inclusion/exclusion criteria, information sources (e.g., MEDLINE), approaches to dealing with monotherapies versus combination therapies, approaches to dealing with potential covariate effect modifiers (i.e., sources of heterogeneity). **RESULTS:** We identified 11 published MTC, of which 7 were published since 2009. We identified major discrepancies in the inclusion of trials, despite highly similar eligibility criteria and literature searches. The total number of trials covered among all MTCs was 61. The number of trials, however, included in the individual MTCs published since 2009 spanned from 15 to 31 – i.e., 25%-50% of all available trials. We identified inconsistencies in approaches to dealing with monotherapy and combination therapy trials. Most MTCs lumped the two sets of trials without either controlling for the effect of concomitant use of disease modifying anti rheumatic drugs (DMARDs) or separately comparing the effectiveness estimates in the two. Approximately half of the identified MTCs did not explore potential sources of heterogeneity. Among those that did, the explored sources were inconsistent. **CONCLUSIONS:** Major methodological shortcomings and inconsistencies exist throughout published rheumatoid arthritis MTCs. There are many lessons to be learned from these previous publications which can potentially strengthen the current evidence base.

PMS86

USE OF COMMON DATA MODEL TO ENABLE MEANINGFUL COMPARISON OF DISEASE BURDEN AMONG DISPARATE DATABASES

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OBJECTIVES: Use of a Common Data Model (CDM) to standardize underlying data assumptions and format enables consistency in the application of research methods and production of meaningfully comparable results across disparate data sources. This study compared the baseline disease burden, as measured via a standard method deriving Charlson Comorbidity Index (CCI), which was applied to multiple observational databases after all source data was transformed into a standard CDM format. **METHODS:** Two unique patient cohorts, 1) newly diagnosed and treated depression patients (DEP), and 2) newly diagnosed rheumatoid arthritis patients (RA) were identified using equivalent definitions from multiple claims databases which had been previously transformed into a standard CDM format. CCI was calculated for each Cohort using a single SAS macro developed for CCI derivation using CDM-format data. Descriptive information on CCI, in aggregate and stratified by age category and gender, was compared separately for the DEP and RA cohorts across all databases. **RESULTS:** Despite a common data format, consistent cohort definitions, and a single method for CCI derivation, the calculated CCI varied by as much as 20% (RA) and 50% (DEP) across the different databases used for this study. Gender had little influence on CCI differential. CCI differential generally decreased with advancing age category for both DEP and RA, with largest differentials exceeding 4-fold in 18-30 age group (DEP) and smallest differentials of 10% in 80+ age group (DEP). **CONCLUSIONS:** Common Data Models provide an efficient way of enabling meaningful comparisons across disparate data sources. Disparities in CCI results, despite identical cohort definitions and the application of a single SAS macro, are likely the result of differences in underlying populations, data capture process, and/or functional ability and/or incentive to record complete information in source data. Future research should focus on how each of these factors may impact disease burden indices.

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OSTEOARTHRITIS IN FRANCE THE COST OF AMBULATORY CARE IN 2010

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OBJECTIVES: In France, the cost of an osteoarthritic patient has not been estimated for several years. The aim of the study was to evaluate the annual cost of the treatment given to osteoarthritic patients by GP. **METHODS:** The cohort was made

up of patients who were diagnosed with osteoarthritis between April 2009 and March 2010 (IMS Disease Analyzer database). The cost includes all medical cost to the patients in the cohort, and colligated in the Disease Analyzer database (all consultations with GPs and all resulting drug prescriptions). The evaluated cost is therefore the annual cost of treatment given to an osteoarthritic patient. **RESULTS:** A total of 18,976 patients suffering from osteoarthritis were followed. For these patients, who had an average age of 66, all consultations with GPs as well as all resulting drug prescriptions were valued both in terms of societal cost and cost to health insurance. The average annual cost of disease management by a GP of a patient suffering from osteoarthritis is therefore valued at €755 societal cost, of which around 60% (€447) is paid by health insurance. The annual cost of treatment by a GP of a patient suffering from hip osteoarthritis is significantly lower at the societal level (€715) than at the health insurance level (€425) compared to patients suffering from osteoarthritis in the knee or elsewhere, despite their higher age. **CONCLUSIONS:** No literary data evaluating the cost of an osteoarthritic patient currently exists. The closest data is that produced by a COART® France study (Le Pen and coll, *Revue du rhumatisme*, December 2005). The prevalence of osteoarthritis has been estimated at around 4 million sufferers, even though this figure may be conservative, we can estimate that the cost of osteoarthritis treatment is around 3 billion euros. We are sure that further data will be added to existing ones.

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MIXED TREATMENT COMPARISON, COST-EFFECTIVENESS ANALYSIS AND BUDGET IMPACT MODEL IN THE TREATMENT OF RHEUMATOID ARTHRITIS AFTER FAILURE OF CONVENTIONAL DMARD THERAPY USING COMPREHENSIVE BAYESIAN DECISION ANALYTICAL MODELLING

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OBJECTIVES: Eighteen percent of patients with rheumatoid arthritis (RA) escape conventional treatment with Methotrexate and hence biological agents like TNF- α inhibitors are also used. Given a population of patients with severe rheumatoid arthritis we sort to assess efficacy and safety after failure of DMARD, to estimate the budget impact of the management of RA in France, to compare between average annual cost of maintaining a patient under treatment and finally to evaluate the cost-effectiveness of different available strategies. **METHODS:** We carried out a systematic review of randomized control trials conducted between 1999 and 2010 on patients with RA on treatment with one of the biological agents, a quantitative synthesis of the evidence from random effects mixed treatment comparison was also done and a Markov model to assess budget impact and cost effectiveness of different strategies was constructed. We assumed that (i) Response, discontinuation and infection rates where constant over time (ii) model results in terms of cost and effectiveness were calculated considering 1st line, 2nd line and both (iii) Evolutionary trends in market shares for the most effective drug where analyzed. Sensitivity analysis was also performed. **RESULTS:** Biotherapy differed significantly from DMARDs in terms of ACR 50 response. Given a willingness to pay of 1,715€ Adalimumab was efficient, beyond this WTP threshold, Etanercept was the most effective treatment. A comparison of an increase or decrease in Etanercept market share shows that the replacement of ETA by more expensive and/or less effective therapies results in a loss estimated at 28million euros over 5years. Considering only 1st or 2nd line of biotherapy, results in a 4.04% increase of average annual cost of managing a patient after failure of DMARDs. **CONCLUSIONS:** Substitution of more expensive biological therapies without additional therapeutic benefit to the patient implies economic loss for society.

PMS89

SIMULATION MODELING WITH SYSTEM DYNAMICS (SD) USING REAL-WORLD OBSERVATIONAL DATA TO PLAN OSTEOARTHRITIS CARE DELIVERY IN ALBERTA

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OBJECTIVES: Currently, there are no reliable and validated methods for health service decision-makers to inform policy on quality care at a systems level. To address this need, we worked with health administrators, clinicians and researchers to create and validate a decision-support tool that service planners can use to achieve a sustainable, integrated care system for hip and knee OA. **METHODS:** The SD model reflects the continuum of care, including self-directed, primary, rheumatologic and orthopaedic specialist for hip and knee replacement, acute, rehabilitation, community and surgical follow-up care. The model was developed in four phases, with phase 1 focusing on demand and flow rates, phase 2 on resources, phase 3 adding geographical stratification, and phase 4 adding feedback loops. We populated the model with administrative data from Alberta Health & Wellness (physician claims, inpatient, and ambulatory data), Survey of Living with Chronic Diseases in Canada, and clinical/surgical data from Alberta Bone and Joint Health Institute. Using established principles of SD modeling and an iterative process of integrated knowledge translation we defined the problem, modeled the system as a series of stock and flows, and validated the model. Through multiple workshops, experts from front-line clinical staff and administrators provided input and improved face validity. **RESULTS:** OA care process diagrams were the preferred format for developing the model structure. The fully specified SD model has been validated with end-users and can be used as a decision-support tool to test scenarios and their resulting effects on system performance and costs. **CONCLUSIONS:** Based on multiple real-world observational data sources, this SD Model allows evaluation of alternative clinical and administrative scenarios that reflect antici-

pated changes in health care demands and service. Furthermore, the integrated knowledge translation process reflects the critical importance of involving clinicians and decision-makers when developing a system dynamics model for applied use.

PMS90

THE INFLUENCE OF 'WEAK LINKS' ON COMPARATIVE TREATMENT EFFECTS IN MULTIPLE TREATMENT COMPARISON META-ANALYSIS: A SIMULATION STUDY

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OBJECTIVES: To investigate the stability of comparative treatment effects in multiple treatment comparison meta-analyses where one sparsely informed treatment comparison (i.e., a 'weak link') constitute the only available evidence for linking two separate clusters of treatments. **METHODS:** We simulated MTC scenarios where two clusters of well-informed treatment comparisons (i.e., each comparison included a large number of trials and patients) were connected by only one sparsely informed comparisons, and where the treatments in one cluster were generally more effective than in the other cluster. As a control, we also simulated scenarios where the two clusters were connected by one well-informed comparison. We varied the degree of heterogeneity and baseline event rates across simulation scenarios. We estimated the probability that the treatments in the cluster of less effective treatments appeared better than to the treatments of the other cluster, as well as the probability that they appeared similar – either judged by their associated treatment rankings or by their comparative 95% credible intervals. **RESULTS:** Treatment rankings were dominated by spurious treatment effect estimates, and depending on the scenario, yielded misleading inferences in 10-30% of MTCs. The 95% credible intervals generally had close to nominal coverage. Thus, the less effective treatments rarely appeared significantly better. Power, however, was typically lower than 20% to detect the superiority of the better treatments. **CONCLUSIONS:** 'Weak links' in MTCs can occur over time when, for example, drug combinations or new classes of drugs are introduced. Although clusters of comparisons (e.g., comparisons amongst drugs belonging to the same class) may be well-informed by several trials and randomized patients, the overall comparative effectiveness between all considered treatments may hinge primarily on a few 'weak links'. When this happens it is important to recognize the statistical limitations demonstrated in our simulations.

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USING DISCRETE CHOICE EXPERIMENTS (DCE) TO ESTIMATE PREFERENCE-BASED UTILITIES FOR DUPUYTREN'S CONTRACTURE (DC)

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OBJECTIVES: Descrete Choice (DC) is a proliferative connective tissue disorder in which fingers bend towards the palm and cannot be fully extended. DC's quality of life impact varies according to number/severity of affected fingers. To overcome this heterogeneity, DCE methods were used to estimate DC utilities. **METHODS:** A sample of the United Kingdom general population was invited, via Internet, to state preferences for varying hypothetical DC hand severity, defined using a combination of contractures (0°, 45° or 90°) in 8 joints [proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints of the index, middle, ring and little fingers]. Using an optimal DCE design, 56 DC hands were selected from the 6,561 (=38) possible profiles. Right-handed, left-handed, and ambidextrous respondents were asked to compare 10 randomly selected profile pairs and to indicate which hand, within each pair, was preferable. To facilitate consistent comparisons, anatomically precise digital hand drawings were used. To anchor preferences on a traditional 0-1 utility scale, participants indicated how having the most severe hand (all joints bent 90°) would affect their EQ-5D-5L profile. Unaffected hands were assumed to have a utility of 1.0. Conditional logistic models were used to estimate indirect utility weights for the joints, and were subsequently rescaled to EQ-5D-5L. **RESULTS:** A total of 1745 participants provided valid and complete responses. Anchoring utilities for the most severe dominant, non-dominant, and ambidextrous hands were 0.4909, 0.5688 and 0.6343, respectively. For a dominant hand with 90° contracture in MCP joints of the ring and little fingers, the estimated utility was 0.8848. If only the MCP joint of the ring finger was affected, the utility was 0.9477 and increased to 0.9738 if the contracture was 45° instead. **CONCLUSIONS:** DC may be associated with relatively large utility decrements. The model provides a convenient and useful tool to estimate any preference-based DC utilities for clinical and economic appraisals.

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ADAPTATION AND VALIDATION OF AN INDIAN VERSION OF THE HEALTH RELATED QUALITY OF LIFE SCALE (IND-HAQ) IN INDIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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OBJECTIVES: To test the validity and reliability of a newly developed Rheumatoid Arthritis (RA) quality of life instrument: the Indian Health-Related Quality of Life Instrument (IND-HAQ). **METHODS:** A total of 60 rheumatoid arthritis (RA) patients were asked to complete the IND-HAQ at 2 time points (4 weeks apart). Patients also completed the Stanford Health Assessment Questionnaire (PROMIS-HAQ) at the second time point. PROMIS-HAQ scores were used to assess the validity of the IND-HAQ. Besides the HAQ, the other outcome measures constituting the ACR